Annals of Clinical and Analytical Medicine
Original Research

Evaluation of serum vitamin D levels in pregnant women with gestational diabetes mellitus

Serum vitamin D assessment in gestational diabetes pregnancy

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Abstract

Aim: This study aims to examine the association of maternal serum 25- (OH)Vitamin D concentrations with gestational diabetes mellitus.

Material and Methods: This single-centered and prospective study included 60 pregnant patients with a diagnosis of gestational diabetes who applied to our hospital between March 1, 2023, and June 1, 2023, for blood sugar monitoring or delivery. The study aslo included a total of 148 patients including pregnant women without gestational diabetes and female patients of similar age who were not pregnant as the control group. All patients ' demographic characteristics, pregnancy information, and medical histories were recorded. 25- (OH)Vitamin D levels were measured in serum samples taken from the patients.

Results: Serum 25-(OH) vitamin D levels were compared between pregnant women with gestational diabetes, pregnant women without gestational diabetes, and non-pregnant female patient groups of the same age. The mean 25-(OH) vitamin D level in the patient group with GDM (10.81±9.24), the mean (10.41±7.49) in the control group without GDM, and the mean in the non-pregnant control group female patients (11.56±7.25) (p= 0.203). Based on these results, there was no statistically significant difference between the groups' 25-(OH) Vitamin D levels. Despite this, vitamin D deficiency was evident in all groups.

Discussion: Vitamin D deficiency is a critical health problem for mothers and newborns. The study investigates the impact of 25-(OH) vitamin D on gestational diabetes (GDM). Despite non-significant differences in vitamin D levels between GDM and healthy pregnant groups, the study highlights the prevalent deficiency across all groups, emphasizing the need for further investigation. In conclusion, the widespread vitamin D deficiency among young women and pregnant individuals calls for continued research to comprehend its implications for GDM.

Keywords

Gestational Diabetes, Vitamin D Deficiency, 25-Hydroxy Vitamin D, Oral Glucose Tolerance Test

DOI: 10.4328/ACAM.22096 Received: 2024-01-15 Accepted: 2024-03-05 Published Online: 2024-03-21 Printed: 2024-05-01 Ann Clin Anal Med 2024;15(5):339-343
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This study was approved by the Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital (Date: 2023-02-07, No: 3797)

Introduction

Gestational Diabetes Mellitus (GDM) is a medical condition affecting pregnant women, characterized by varying degrees of glucose intolerance. This condition poses risks to both the mother and the fetus, regardless of whether it is treated with dietary modifications or insulin therapy and even if it persists after pregnancy. The increasing prevalence of GDM over recent years has raised public health concerns.

Vitamin D is a fat-soluble vitamin critical in several physiological processes, including bone health [1]. However, recent studies suggest that vitamin D deficiency could contribute to the onset and progression of diabetes. Additionally, emerging evidence indicates that vitamin D deficiency could significantly impact the pathogenesis and management of GDM [2].

The present study aims to investigate the potential effects of vitamin D deficiency on GDM by comparing the serum vitamin D levels of GDM patients to those of healthy pregnant and non-pregnant women in the same age group. We also aim to emphasize the importance of routine evaluation of vitamin D levels during pregnancy assessments.

Furthermore, the study aims to identify the significance of preventive measures for GDM during pregnancy. By conducting a comprehensive review of existing literature and assessing current evidence, we hope to provide insights into the potential clinical outcomes associated with vitamin D deficiency in the context of gestational diabetes mellitus.

Material and Methods

Selection and Description of Participants

Our study, conducted between Mar 1, 2023, and Jun 1, 2023, included 60 pregnant patients diagnosed with gestational diabetes mellitus at the Şişli Hamidiye Etfal Training and Research Hospital's Obstetrics and Gynecology Clinic. Additionally, 88 pregnant individuals without gestational diabetes mellitus, matched for age, and 60 non-pregnant women were selected as the control group to compare serum D vitamin levels. Demographic details such as age, gravidity, parity, week of admission, indication for admission, and BMI were obtained from the hospital's electronic file system and through detailed patient history.

All participants were provided comprehensive information about the study, and verbal consent was obtained.

Inclusion Criteria

- Pregnant individuals aged 18-40 years.
- İndividuals for whom clear information is accessible through file screening, as well as Oral Glucose Tolerance Test results available between the 24th and 28th weeks of pregnancy.

Control Group Criteria

- Pregnant individuals with normal Oral Glucose Tolerance Test results who were admitted for childbirth or pregnancy follow-up.
- Non-pregnant women aged 18-40 years who visit the hospital's outpatient clinic.

Exclusion Criteria

- Pregnant individuals aged below 18 or above 40 who are admitted for childbirth or pregnancy follow-up.
- Pregnant individuals who did not undergo the Oral Glucose Tolerance Test between the 24th and 28th weeks of pregnancy.
- Patients with incomplete information in the hospital electronic file system.
- Patients with known diagnosis of diabetes before pregnancy.
- Patients who use medications affecting calcium and vitamin D metabolism during pregnancy (excluding routine prenatal multivitamins).
- Patients with chronic diseases related to thyroid, parathyroid, or kidney.
- Patients with multiple pregnancies.

Technical Information

The study utilized a 75-gram Oral Glucose Tolerance Test for gestational diabetes mellitus diagnosis. Testing appointments were scheduled for patients in their 24-28th weeks of pregnancy. After 12 hours of fasting, blood samples were taken for fasting serum glucose. Subsequently, patients ingested a 75-gram glucose solution, and blood samples were collected at 1 and 2 hours post-ingestion.

OGTT Cut-off Values

Fasting: 92,
1st Hour: 180,
2nd Hour: 153.

Venous blood samples for D vitamin determination were centrifuged and stored at -80°C until analysis. D vitamin levels were measured using a chemiluminescent immunoassay with the Centaur XP (Siemens Healthcare United Kingdom) device. Cutoff values for D vitamin levels were defined as follows:

<12: D vitamin deficiency,
12-20: D vitamin insufficiency,
>20: Adequate D vitamin levels.

Statistics

Statistical analysis was performed using SPSS 15.0 for Windows. Descriptive statistics included counts and percentages for categorical variables and mean, standard deviation, minimum, maximum, and median for numerical variables. Due to the non-normal distribution of numerical variables, the Mann-Whitney U and Kruskal-Wallis tests were used for independent two-group and multiple-group comparisons. Subgroup analyses were conducted using the Mann-Whitney U test with Bonferroni Correction. Proportions in groups were compared using the Chi-square test. ROC Curve analysis was employed for threshold value assessments. The statistical significance level was set at $p<0.05$.

Ethical Approval

This study was approved by the Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital (Date: 2023-02-07, No: 3797)

Results

The study included 56 pregnant women diagnosed with gestational diabetes mellitus (GDM), 82 healthy pregnant women, and 58 healthy non-pregnant women, all subjects for comparison based on 25-(OH) D vitamin levels.

The mean age of the GDM group was statistically lower than that of the control group ($p=0.037$), and the parity number was significantly reduced compared to the control group ($p=0.020$). The Cesarean section rate in the GDM group was higher than in the control group.

Statistical analysis revealed significant differences in various

parameters among the GDM, OGTT normal pregnant, and Control groups. These included age, gravida, parity, abortion numbers, mode of delivery, the week when GDM diagnosis was established, and the week of hospitalization (p=0.001, p=0.028, p=0.018, p=0.016, p=0.009, p=0.033, p=0.009, p<0.001, p<0.001, p<0.001).

The average age of the OGTT normal pregnant group was statistically lower than the GDM and control groups (p=0.002). Regarding gravida, the GDM group had a significantly higher average than the control group. Parity in the OGTT normal pregnant group was statistically lower than in the control group, and the GDM group's abortion average was significantly higher than the OGTT normal pregnant group (p=0.021, p=0.009, p=0.005).

The week of OGTT in the GDM group was statistically later than in the OGTT normal group. The week of hospitalization in the GDM group was lower than the OGTT normal pregnant group. OGTT 0-60-120 min blood sugar averages were higher in the GDM group compared to the OGTT normal pregnant group.

No statistically significant differences were found in the average serum D vitamin levels and the ratio of D vitamin <20 among groups (p=0.203, p=0.689). Additionally, no significant differences were observed in vitamin D levels and BMI.

In the OGTT normal pregnant group, the serum D vitamin level showed a very weak positive correlation with the patient's age and a very weak negative correlation with the week of hospitalization during pregnancy. In the GDM group, a moderately positive correlation was found between OGTT 60 min level and serum D vitamin. In the OGTT normal pregnant group, a very weak negative correlation was observed between the week of prenatal hospitalization and serum D vitamin (p=0.037, p=0.042, p=0.035, p=0.032).

Discussion

Gestational Diabetes (GDM) is a carbohydrate intolerance that begins or is first noticed during pregnancy. In addition to affecting approximately 14% of the entire pregnant population, it is crucial to know maternal and fetal complications and to investigate protective mechanisms that can be prevented. To examine the role of 25-(OH) vitamin D in the pathogenesis of GDM during pregnancy, to identify patients in the risk group, and to improve pregnancy outcomes, we planned to investigate the importance of 25-(OH) vitamin D supplementation and shed light on future studies with the results we found.

Studies conducted in healthy individuals have shown an inverse relationship between serum 25-(OH) Vitamin D level, glucose concentration, and insulin resistance [3]. In the study by Agarval et al., the relationship between serum 25-(OH) Vitamin D levels and insulin resistance was examined in 71 non-diabetic postmenopausal women; there was a negative correlation between insulin resistance (HOMA-IR; homeostasis model assessment of insulin resistance) and 25-(OH) Vitamin D [4]. Additionally, observational studies have found an association between vitamin D levels and Type 2 DM. In a meta-analysis of 21 prospective studies evaluating the relationship between serum 25-(OH) Vitamin D levels and the incidence of type 2 DM,

Table 1. Comparison of GDM and Control Groups in Terms of Demographic and Clinical Characteristics

		GDM Group	OGTT Normal Group	Control Group	p
		Ort.±SD Min-Max (Median)	Ort.±SD Min-Max (Median)	Ort.±SD Min-Max (Median)	
Age		32,4±5,6 18-41 (33,5)	29,3±5,9 18-42 (29)	32,4±6,2 20-41 (34)	0,001
G		2,52±1,51 1-8 (2)	1,96±1,04 1-5 (2)	1,90±1,88 0-7 (2)	0,028
P		1,10±1,00 0-3 (1)	0,80±0,88 0-3 (1)	1,61±1,65 0-6 (1)	0,018
A		2,18±1,17 1-5 (2)	1,20±0,41 1-2 (1)	2,00±1,15 1-4 (2)	0,016
Type of Delivery	Vaginal	14 (23,3)	20 (22,5)	26 (42,6)	0,009
	C/S	21 (35,0)	27 (30,3)	8 (13,1)	
	Vaginal+C/S	4 (6,7)	1 (1,1)	2 (3,3)	
	Nulliparous	21 (35,0)	41 (46,1)	25 (41,0)	
BMI		30,8±5,3 22-59 (30)	29,6±3,9 21-39 (30)	30,2±5,5 16-45 (31)	0,619
Week of GDM Diagnosis		24,9±1,3 24-30 (24)	24,4±0,9 24-29 (24)		0,033
Patients' Hospitalization	Week	35,5±3,9 24-41 (36,5)	37,0±3,3 25-42 (38)		0,009
	Day	2,90±2,1 0-6 (3,5)	2,6±2,1 0-6 (2)		0,403
OGTT 0		108,2±32,7 67-250 (98)	84,5±5,5 70-92 (85)		<0,001
OGTT 60'		181,8±13,7 164-206 (185)	132,2±19,2 87-178 (133)		<0,001
OGTT 120'		143,3±25,6 86-168 (154)	106,8±18,2 47-151 (110)		<0,001
Treatment	Insulin	11 (18,3)			
	Diet	49 (81,7)			
	None	-	89 (100)		
Serum Vitamin D Levels		10,81±9,24 3-41,9 (8,285)	10,41±7,49 3-36 (8,5)	11,56±7,25 3-39,6 (9,26)	0,203
Serum Vitamin D	≤20	51 (85,0)	78 (87,6)	55 (90,2)	0,689
	>20	9 (15,0)	11 (12,4)	6 (9,8)	
Serum Vitamin D	<12	43 (71,7)	62 (69,7)	38 (62,3)	0,478
	12-20	8 (13,3)	16 (18,0)	16 (26,2)	
	>20	9 (15,0)	11 (12,4)	7 (11,5)	

it was stated that there was a negative and positive relationship between serum 25-(OH) Vitamin D and the incidence of Type 2 DM [5].

One of the most critical risk factors for the development of GDM and Type 2 DM is obesity. Obesity has also been associated with hypovitaminosis D. This can be explained by the fact that vitamin D cannot be converted into its active form because it is stored in fat tissue.

In a study evaluating the relationship between serum 25-(OH) Vitamin D levels and insulin resistance in healthy overweight and obese individuals, serum 25-(OH) Vitamin D levels and Body Mass Index (BMI), waist circumference, fasting plasma insülin, and HOMA-IR values are in a negative relationship, and it has been determined that low serum 25-(OH) Vitamin D levels in obese individuals are responsible for insulin resistance or hyperinsulinemia [6]. Our study did not find a statistically significant relationship between the patient and control groups' vitamin D levels and BMI parameters.

In the study conducted by Lacroix et al., which included 655 pregnant women, 25-(OH) Vitamin D levels were measured in the first trimester, and blood glucose and insulin values were examined in the second trimester. Based on IADPSG criteria, GDM was detected in 8.2% of the participants. Low vitamin D levels in the first trimester were found to be significantly associated with the development of GDM, and vitamin D deficiency was interpreted as an essential factor in the development of GDM [7].

According to the meta-analysis by Zhang et al., pregnant women with maternal GDM had statistically significantly lower vitamin D levels compared to other healthy pregnant women. Still, it was also emphasized that there would be regional differences [8]. Similar to this meta-analysis, studies conducted in healthy individuals in the literature have shown an inverse relationship between serum 25-(OH) Vitamin D level, glucose concentration, and insulin resistance [9]. It has also been shown in further studies that vitamin D has a role in the pathogenesis of diabetes. In a cross-sectional survey of Soheilykhah et al., 24-28. Serum 25-(OH) Vitamin D levels were lower in GDM women than in non-diabetic pregnant women during the gestational weeks [10].

In another study by Clifton-Bligh et al., maternal serum 25-(OH) Vitamin D concentrations measured during GDM screening testing were significantly and inversely associated with fasting glucose. Still, the association of vitamin D with GDM risk was not statistically significant.

Again, as a result of a study conducted by Farrant and colleagues in an Indian population, it was revealed that there was no significant relationship between 25-(OH) Vitamin D concentrations and GDM risk [13]. Our findings are also compatible with these two studies.

In a study conducted by Parildar et al. to evaluate the frequency of vitamin D deficiency in pregnant women and the relationship of vitamin D deficiency with glucose parameters and the incidence of gestational diabetes, 42 pregnant women with GDM and 78 pregnant women without GDM were evaluated. Serum 25-(OH) Vitamin D levels of all individuals were assessed, and serum 25-(OH) Vitamin D level <20 ng/mL was determined as vitamin D deficiency [12]. The prevalence of vitamin D deficiency in the women with GDM and the control group participating in the study was statistically significantly different. In individuals with GDM (n=42), no significant difference was detected between the fasting plasma glucose, fasting insulin, and HbA1c levels of the group with and without vitamin D deficiency.

In a study conducted in the Istanbul region, the average vitamin D level in 44 pregnant women in the first three months of pregnancy was 11.1±3.80 ng/mL. Vitamin D was found below 10 ng/ml in 70.45% of the cases [11].

According to the results of our study, serum vitamin D levels were not different in the three groups (p = 0.203). However, vitamin D levels were found to be deficient in healthy pregnant women (mean±SD; 10.1±7.49 µg/L), gestational diabetic pregnant women (10.81±9.24 µg/L), and healthy young women (11.56±7.25 µg/L), that is, in all groups (Table 1). 25-(OH) vitamin D level; Deficiency (≤12 µg/L) was found in 71% of pregnant women with GDM, insufficiency (12-20 µg/L) in 13%, and sufficiency (20-32 µg/L) in 14%. Healthy pregnant women: It was found to be deficient in 69%, insufficient in 18%, and at the proficiency level in 12%. Healthy young women were found to be deficient in 62%, inadequate in 26%, and at a sufficient level in 11% (Table 1).

In studies conducted on 559 pregnant women in India and 76 pregnant women in the Czech Republic, vitamin D levels were not found to be different in gestational diabetic pregnant women and healthy pregnant women. In contrast, vitamin D levels were found to be deficient in both groups of pregnant women [11].

Similar to all these results, while we could not find a statistically significant difference in vitamin D levels between the gestational diabetic and the healthy pregnant groups, we detected a high rate of vitamin D deficiency in both groups. In this study, we found vitamin D levels deficient in healthy pregnant women, gestational diabetic pregnant women, and healthy young women, that is, in all groups. This study revealed that vitamin D deficiency is common in our region as well as all over the world and in our country. While severe (≤12 µg/L) vitamin D deficiency is observed in 70% of pregnant women with GDM and healthy pregnant women and in 62% of healthy young women, Vitamin D deficiency (12-20 µg/L) in all groups averaged 19%. The average number of women with adequate vitamin D levels (20-32 µg/L) in all three groups is 12%. In light of these results, we see that vitamin D deficiency is a noticeable problem in both pregnant and non-pregnant women.

Limitation

As a few limitations of our study, serum 25-(OH) Vitamin D concentrations taken in the late trimester may not indicate maternal vitamin D status throughout the entire pregnancy period and, therefore, may be misleading in determining the relationship between the development of GDM and vitamin D status. In addition, another limitation was that we needed more patients and control groups compared to studies on similar subjects.

As a result of this study, we attributed the lack of a significant difference in vitamin D deficiency in patients with and without GDM to the high prevalence of Vitamin D deficiency. We attributed the frequent occurrence of vitamin D deficiency to the geographical characteristics of our country.

Conclusion

As a result, vitamin D deficiency is widespread in young women and all pregnant women. It is associated with many complications, such as preeclampsia, gestational diabetes, premature birth, impaired glucose tolerance, and increased cesarean section rate. Although the importance of multivitamin supplementation during pregnancy is evident, more studies are needed to reveal the relationship between the effect of vitamin D deficiency on the development of gestational diabetes.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

Funding: *None*

Conflict of Interest
The authors declare that there is no conflict of interest.

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How to cite this article:
Narin Ece Çakmak, Burak Çakmak, Gül Özel Doğan, Alev Atış Aydın. *Evaluation of serum vitamin D levels in pregnant women with gestational diabetes mellitus. Ann Clin Anal Med 2024;15(5):339-343*

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